PATENT
8012-1317

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Satoshi OMURA et al. Conf. 5881

Application No. 10/532,662 Group 1654

Filed January 19, 2006 Examiner M. Audet

NOVEL SUBSTANCE FKI-1033 AND PROCESS
FOR PRODUCING THE SAME

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

December 3, 2007

Applicants request a pre-appeal brief review of the final rejection in the above-identified application. No amendments are being filed with this request.

A Notice of Appeal is filed herewith.

The review is requested for the reasons advanced on the attached sheets.

Respectfully submitted,

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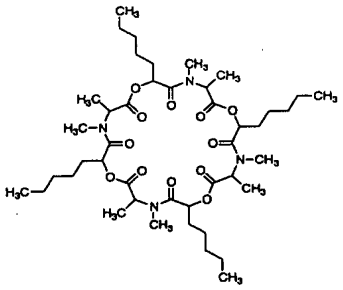
REASONS IN SUPPORT OF REQUEST FOR REVIEW

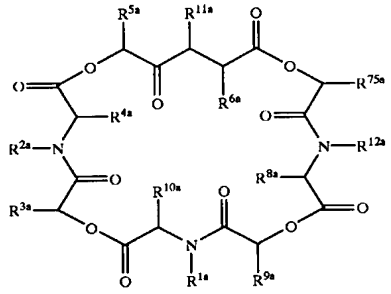
The claims are directed to a substance FKI-1033:



Claims 1, 7-10 and 13-15 are not anticipated by KALBE et al. WO 01/62268 A1, as evidenced by its U.S. equivalent US 2003/0125244 A1 (US '244), or KALBE et al. WO 02/00202 A1, as evidenced by its U.S. equivalent US 2004/0043925 A1 (US '925).

Each WIPO publication discloses 6-30 atom ring or chain depsipeptides, preferably an 18-24 atom ring, in particular:

(Ia)



The position of the Official Action is that formula Ia anticipates the claims because each publication discloses "C_1 alkyl (methyl)" for each of R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} and "C_5 alkyl (pentyl)" for R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a}.

MPEP 2131.02 states that for the holding of anticipation a claimed species must be "at once envisaged" from a

generic formula disclosed by a reference. However, it is not possible to "at once envisaged" FKI-1033 from the vast number of species suggested by the generic formula of the publications, herein "KALBE".

KALBE discloses "methyl" as one of many possible R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} groups, and "straight-chain or branched C_1-C_8 alkyl", "optionally substituted", as one of many possible R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a}. There is no explicit disclosure of a "straight chain C_5", not substituted, i.e., n-pentyl. See, e.g., US '244,para. 53-67 or US '925, para. 52-65.

Even in the most concise "particular preference", KALBE fails to provide sufficient guidance to even approach the claimed FKI-1033. TABLE 1 illustrates possible structures for each "R" in the "particular preference".

TABLE 1

Set	Possible structures for each "R"
R^{1a} R^{2a} R^{11a} R^{12a}	**7 structures:** • 7 identified alkyls: methyl, ethyl, propyl, isopropyl, n-, s-, and t-butyl
R^{3a} R^{5a} R^{75a} or R^{7a} R^{9a}	**>>80 structures:** • Hydrogen • 49 named alkyls optionally substituted with named groups(i.e., methyl, ethyl, propyl, isopropyl, n-, s-, t-butyl substituted with 1 of 6 named groups) • 24 straight chain C_5,C_6,C_7,C_8 alkyl groups, optionally substituted with the 6 named groups • 6 aromatic groups optionally substituted (i.e., 3 aromatics substituted with 1 named group) Plus a vast number of other possible structures, including: • branched C_5,C_6,C_7,C_8 alkyl groups, optionally substituted with one of 6 named groups or unnamed groups • methyl, ethyl, propyl, isopropyl, n-, s-, t-butyl, and 3 aromatics substituted with unnamed groups
R^{4a} R^{6a} R^{8a} R^{10a}	**> 44 structures:** • Hydrogen • >36: methyl, ethyl, n-propyl, n-butyl, vinyl, and cyclohexyl, each optionally substituted with 6 named groups or unnamed groups • 2: isopropyl and s-butyl >6: phenyl, benzyl, or phenylethyl, optionally halogen-substituted

Thus, in order to even approach the claimed invention one would have been forced to pick and choose, without any guidance from KALBE the following: 1 of 2401 (i.e., 7^4) sets of R^{1a}, R^{2a}, R^{11a} and R^{12a} to arrive at 4 methyl groups, 1 of more than 3,748,096 (i.e., $(>44)^4$) sets of R^{4a}, R^{6a}, R^{8a}, and R^{10a} to arrive at 4 non-substituted methyl groups, and 1 of more than 40,960,000 (i.e., $(>>80)^4$) sets of R^{3a}, R^{5a}, R^{75a} or R^{7a} and R^{9a} to arrive 4 non-substituted n-pentyl groups.

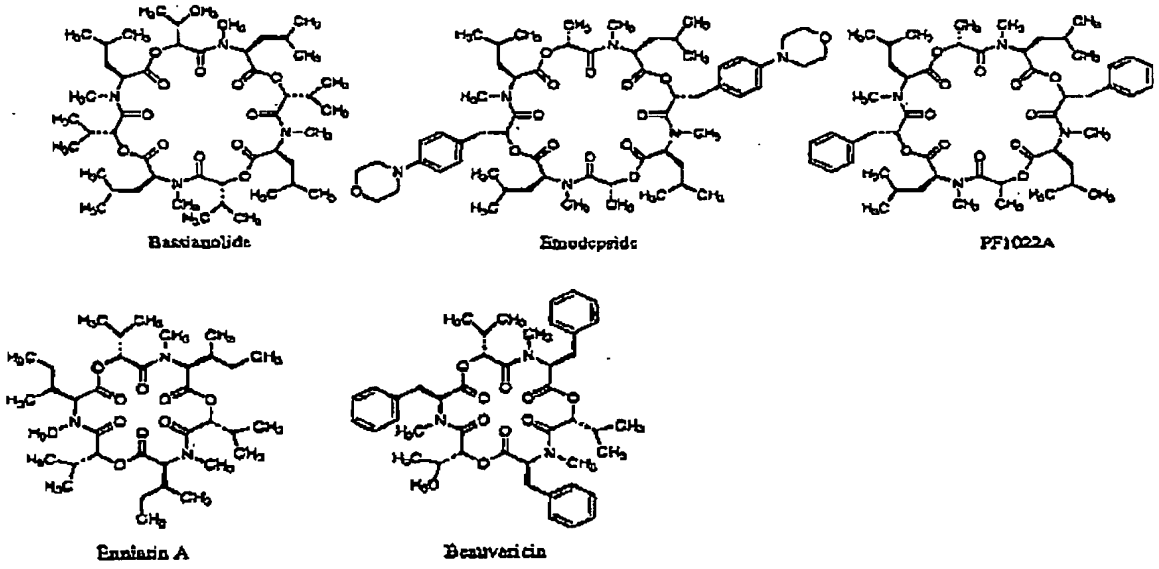
The Examiner is reminded that a generic formula which encompasses a vast number of compounds does not describe and thus anticipate all compounds embraced there in merely because they are within the scope of the formula. *In re Petering et al.* (CCPA 1964) 301 F.2d 676, 133 USPQ 275; *E.I. DuPont de Nemours & Co. v. Ladd, Comr. Pats., et al.* (CADC 1964) 328 F.2d 547, 140 USPQ 297. There can be no anticipation where the reference is so broad that the likelihood of arriving at the claimed composition would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey* (POBA 1939) 41 USPQ 583; *Ex parte Starr* (POBA 1938) 44 USPQ 545, nor is anticipation made out by a hindsight selection based on an applicant's disclosure of variables of a broad generic disclosure. *In re Ruschig et al.* (CCPA 1965) 343 F.2d 965, 145 USPQ 274.

Therefore, in view of the vast number of possible species disclosed by the generic formula of the "particular preference" alone, KALBE cannot possibly anticipate the claims.

Neither does KALBE render obvious the claims.

In addition to failing to disclose or suggest a preference for a species of formula Ia that resembles FKI-1033, KALBE fails to disclose or suggest a species of formula Ia that is isolated from a cultured mass of a microorganism from the *Verticillium* genus of fungi, as recited in claims 15-19, or one that has ryanodine binding inhibition activity, as recited in claims 7, 9, 10 and 13-15.

KALBE discloses that species of formula Ia have good endoparasiticidal activities. However, KALBE fails to recognize the superior unexpected ectoparasiticidal (anthropodicidal) activities obtained from the claimed FKI-1033. The Rule 132 Declaration of April 4, 2007 compared to FKI-1033 to formula Ia species and18 ring depsipeptides:



The toxicity of FKI-1033 against adult cattle ticks was compared to the toxicity of a "particularly preferred" formula Ia

species, i.e., emodepside, of KALBE (See, e.g., paragraph 48 of US '244). In emersion tests, FKI-1033 killed 100% of ticks at 20 µg/ml, but emodepside killed 0% at 100 µg/ml. In injection tests, FKI-1033 killed 100% of the ticks at 0.16 µg/ml, and emodepside killed 100% at 20 µg/ml. Thus, FKI-1033 is unexpectedly more potent than a preferred species of KALBE's formula Ia in anthropodicidal activity. (See, e.g., item 1 of the declaration.)

KALBE also fails to recognize species of formula Ia have a ryanodine binding inhibition activity. FKI-1033 unexpectedly showed 50% ryanodine binding inhibition activity against the American cockroach ryanodine receptor at 4.2 µM, whereas other species of formula Ia showed no binding inhibition at 110 µM, e.g., bassianolide and PF1022A, or PF 1022 as disclosed by KALBE, and 18-ring cyclic depsipeptides (enniatin A and beauvericin). (See, e.g., item 2 of the declaration):

Thus, as KALBE fails to recognize the unexpected superior properties of FKI-1033, as well as that it may be isolated from a cultured mass of a microorganism from the *Verticillium* genus of fungi, the claims cannot be rendered obvious by KALBE.

Conclusion

For the reasons discussed above, the rejections include clear factual and/or legal errors and should be withdrawn. Allowance of the application is, thus, respectfully requested.